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Visual memory and psychotic symptoms in youth

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Abstract

Background: Psychotic symptoms are common during childhood and adolescence and may indicate transdiagnostic risk of future psychiatric disorders. Lower visual memory ability has been suggested as a potential indicator of future risk of mental illness. The relationship between visual memory and clinician-confirmed definite psychotic symptoms in youth has not yet been explored.

Methods: We examined visual memory and psychotic symptoms among 205 participants aged 7-27 years in a cohort enriched for parental mood and psychotic disorders. We assessed visual memory using the Rey Complex Figure Test (RCFT) and psychotic symptoms using validated semi-structured interview measures. We tested the relationship between visual memory and psychotic symptoms using mixed-effects logistic regression.

Results: After accounting for age, sex, and family clustering, we found that psychotic symptoms were significantly associated with lower visual memory (OR = 1.80, 95% CI 1.06 to 3.06, p = 0.030). This result was unchanged after accounting for general cognitive ability.

Conclusion: Lower visual memory performance is associated with psychotic symptoms among youth, regardless of general cognitive ability. This finding may inform future targeted early interventions.

Keywords: cognition; visual memory; psychotic symptoms; youth at-risk

Introduction

Psychotic symptoms, including hallucinations and delusions, are the hallmark of schizophrenia and other psychotic disorders. Transient psychotic symptoms are common in the general population with estimates of 17% among children and 7.5% among adolescents in the absence of any psychotic disorder (Kelleher et al., 2012). Psychotic symptoms in childhood and adolescence predict increased risk of psychotic disorders in adulthood (Poulton et al., 2000). Psychotic symptoms during childhood are an established risk factor for future psychopathology (Fisher et al., 2013; Poulton et al., 2000), with more persistent symptoms being more predictive than transitory ones (Dominguez et al., 2011; Downs et al., 2013). However, not all youth with psychotic symptoms will develop mental illness by adulthood. Thus, it may be beneficial to identify additional risk markers that can improve the ability to predict which youth are at increased risk of major mood and psychotic disorders.

Lower cognitive performance has been demonstrated among individuals with psychotic disorders across many domains of cognition including executive functioning, processing speed, and both verbal and visual memory (Bora & Özerdem, 2017; Frangou et al., 2005; Grimes et al., 2017; Heinrichs & Zakzanis, 1998). Individuals in both the early stages of psychosis and with long-standing psychotic illness have demonstrated lower visual memory ability in comparison to controls (Addington & Addington, 2002). Among youth with a family history of psychotic disorders, lower cognitive ability has been associated with increased risk of illness (Keshavan, 2009). Specifically, lower visual memory performance has been associated with risk of schizophrenia and bipolar disorder among youth with a family history of these disorders (Maziade et al., 2011; Sánchez-Gutiérrez et al., 2019). It is important to identify and characterize the cognitive profile of individuals at high risk of mood and psychotic disorders to allow for the

development of appropriate pre-emptive early interventions (Tyrer, 2013). Poorer visual memory performance may indicate elevated risk for mental illness, especially among youth at familial high risk who are experiencing psychotic symptoms. However, it is unknown if visual memory is poorer in children and adolescents who experience psychotic symptoms without meeting criteria for a psychotic disorder.

The link between psychotic symptoms and cognitive performance in youth has been examined, but there have been some inconsistencies across studies. It has been shown that lower general cognitive ability and theory of mind, but not executive functioning, at age 5 is associated with psychotic symptoms at age 12 (Polanczyk et al., 2010). In contrast, another study found that youth with questionnaire measured psychotic-like experiences exhibit slightly lower general cognitive ability, memory, and executive functioning in comparison to youth without psychotic-like experiences (Cullen et al., 2010). Additionally, we have recently shown that 'hot' executive functions, involving emotion and motivation, are poorer among youth with psychotic symptoms but that there is no difference in performance on tasks assessing 'cold' executive functions, which do not involve emotion (MacKenzie et al., 2017). Conversely, lower processing speed at age 8 and lower attention at age 11 were weakly associated with psychotic symptoms at age 12 in a large birth cohort of children and youth. This study did not find differences in working memory or reasoning and problem solving between youth with and without psychotic symptoms (Niarchou et al., 2013). While the literature on cognition in youth with psychotic symptoms is growing, there is not yet a consensus. It is important to study cognition of youth with psychotic symptoms particularly visual memory to better understand the neurocognitive mechanisms underlying psychotic symptoms and to inform potential early interventions.

In the present study, we aimed to explore the relationship between visual memory performance and psychotic symptoms. We assessed visual memory using the Rey Complex Figure Test (RCFT) and we assessed psychotic symptoms using validated semi-structured interviews in a cohort enriched for offspring of parents with mood and psychotic disorders. We hypothesized that lower visual memory performance would be significantly associated with the presence of psychotic symptoms.

Materials and Methods

Participants

We examined visual memory and psychotic symptoms in 205 participants (102 females and 103 males) from the Families Overcoming Risks and Building Opportunities for Well-Being (FORBOW) cohort. FORBOW is enriched for offspring of parents with major mood and psychotic disorders (Uher et al., 2014). We included 7-27 year old participants who completed the RCFT and diagnostic interviews to assess psychotic symptoms and all Axis 1 disorders. We excluded participants with any known major genetic anomalies (e.g. 22q11 deletion syndrome), neurological illness (e.g. epilepsy), or intellectual disability of a degree incompatible with completing the assessments. This study was approved by the Nova Scotia Health Authority Research Ethics Board (file number 100 266) and complies with the Helsinki Declaration of 1975, revised in 2008. Participants with capacity to make an informed decision provided written informed consent. For participants who could not provide informed consent, participants provided assent and a parent or guardian provided written informed consent.

Visual memory

Visual memory refers to the process by which visual stimuli is stored and recalled through perceptual processing, encoding, storage, and retrieval of such stimuli (Riou et al., 2011). We assessed visual memory using RCFT. The RCFT asks participants to copy a complex figure onto a separate piece of paper and then draw the figure again from memory. In the present study, participants were asked to draw the figure from memory 3 minutes (immediate recall) and then again 30 minutes (delayed recall) after last seeing it. After the participants completed the delayed recall, they completed a recognition recall trial where they were asked to look at 24 images and identify which images were part of the original figure they copied. To ensure consistency across

scoring, a single rater (EHV) who was blind to the outcome, scored all of the RCFTs. We used the quantitative scoring system (Meyers, J. & Meyers, K., 1995) to score the RCFT. This method has been shown to have a median inter-rater reliability coefficient of 0.94 (Shin et al., 2006). Normative scores are available for ages 6-89 (Meyers, J. & Meyers, K., 1995). Consistent with previous studies, we used the delayed recall as the primary measure of visual memory. We defined visual memory using the delayed recall score of the RCFT as previous studies have demonstrated that delayed recall on the RCFT can discriminate between individuals with and without psychotic disorders and with and without a family history of psychotic disorders (Ha et al., 2012; Maziade et al., 2009).

Offspring psychopathology

We assessed offspring for psychiatric disorders using semi-structured interviews with offspring and their parents. For offspring ages 6-18 years, we used the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997) and for offspring ages 18+ years, we used the Structured Clinical Interview for DSM-5 (SCID-5) (First, 2015). Youth assessors were separate from parent assessors and were blind to parent psychopathology. We confirmed offspring diagnoses in consensus meetings with a psychiatrist or psychologist who was blind to parent psychopathology. We measured depressive symptoms using a continuous score from the Mood and Feeling Questionnaire Short Form (MFQ-S) (A Angold et al., 1995).

General cognitive ability

We measured general cognitive ability using full-scale intelligence quotient (FSIQ) derived from the Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II)(Wechsler, 1999) for all participants. The WASI-II FSIQ combines scores from four subtests:

block design, vocabulary, matrix reasoning, and similarities. The WASI-II was administered and double scored by assessors trained in administration and scoring.

Psychotic symptoms

We defined psychotic symptoms as the presence of definite hallucinations or delusions reported on developmentally appropriate interview measures. Assessors were research staff trained and supervised by psychiatrists. We comprehensively assessed psychotic symptoms with validated instruments, including the K-SADS interview (age 6-18 years) (Kaufman et al., 1997), SCID-5 interview (age 18+ years) (First, 2015), Funny Feelings interview (ages 7+ years) (Polanczyk et al., 2010; Poulton et al., 2000), and the Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 2003) (ages 12+ years). These instruments consist of direct questions about the presence of hallucinations and delusions in the 12 months prior to the interview, followed by probing to establish the content and context of each experience. We administered the semi-structured psychosis module of K-SADS or SCID-5 to all participants based on age. The Funny Feelings interview consists of seven direct questions and probes of distress, frequency, and appraisal. SIPS is a semi-structured interview designed to assess early symptoms of psychotic illness. All reported psychotic symptoms were transcribed verbatim and evaluated through curation by an independent psychiatrist or psychologist who was not involved in the assessment of the participant and was blind to parent psychopathology. Psychotic symptoms were present if they were rated as ‘definite’ by independent curation (Polanczyk et al., 2010; Poulton et al., 2000). Ratings of psychotic symptoms in the year when the RCFT was administered were included in analyses.

Statistical analyses

To test the relationship between visual memory and psychotic symptoms, we implemented generalized linear latent and mixed models (GLLAMM) (Rabe-Hesketh & Skrondal, 2016) logistic regression. RCFT delayed recall standard scores were used as the independent variable and psychotic symptoms as the dependent variable. Since we expected poorer performance to be associated with psychotic symptoms, we z-scored and inverted the age-standardized RCFT delayed recall scores so that higher numbers reflected worse performance. We coded the presence of psychotic symptoms as yes = 1 for a participant who reported psychotic symptoms on any of the psychotic symptom measures (K-SADS, SCID-5, Funny Feelings, or SIPS) during the 12 months prior to the assessment of psychotic symptoms and administration of the RCFT. We coded this variable as no = 0 if the participant did not report psychotic symptoms in the 12 months prior to the assessment. We included sex and age as fixed effect covariates. To account for clustering of participants within families, we used the family identifier as a random effect. We conducted sensitivity analyses to ensure that our results were not unduly affected by general cognitive ability (IQ) or the presence of neurodevelopmental disorders (attention-deficit/ hyperactivity disorder (ADHD) or autism spectrum disorder (ASD)) or the presence of major depressive disorder in the offspring. We report the odds ratios (OR), their 95% confidence intervals, and p-values. We interpreted results with p-values below 0.05 as statistically significant. All analyses were completed using STATA 15.1 software.

Results

Demographic and clinical characteristics

Of our participants, 10.73% reported definite psychotic symptoms within the 12 months prior to assessment. Among our 205 participants, 2 participants had a diagnosis of bipolar disorder (1 with psychotic symptoms and 1 without), 1 participant had a diagnosis of schizophrenia, and 28 participants had a diagnosis of major depressive disorder. Thus, we explored the potential role of a diagnosis of major mood and psychotic disorders and the role of depressive symptoms on our results in sensitivity analyses. Our results remain unchanged when we exclude participants with bipolar disorder, schizophrenia, and those with a major depressive episode in the year prior to cognitive testing (please see Supplementary Table 1). Table 1 presents the demographic and clinical characteristics of the participants.

The relationship between visual memory and psychotic symptoms

After accounting for age, sex, and family clustering, worse visual memory was significantly associated with the presence of psychotic symptoms (OR = 1.80, 95% CI 1.06 to 3.06, p = 0.030; Table 2). Figure 1 shows the means and standard errors of RCFT delayed recall scores among participants with and without psychotic symptoms.

Sensitivity analyses

We performed sensitivity analyses to explore whether the above result may have been affected by general cognitive ability (IQ), a diagnosis of ADHD, a diagnosis of ASD, depressive symptoms, and RCFT recognition score (please refer to Supplementary Tables 2-6 in the Supplementary Materials). After accounting for sex, age, and general cognitive ability, the results remained unchanged (OR = 1.87, 95% CI 1.07 to 3.27, p-value = 0.029). When we controlled for ADHD,

ASD, and current depressive symptoms, the association between visual memory and psychotic symptoms remained within one standard error of the original result (controlling for ADHD: OR = 1.70, 95% CI 1.00 to 2.89, p-value = 0.050; controlling for ASD: OR = 1.81, 95% CI 1.06 to 3.09, p-value = 0.030; controlling for depressive symptoms: OR = 1.78, 95% CI 1.04 to 3.03, p-value = 0.035). When we accounted for RCFT recognition ability, our result was also within one standard error of the original result (OR = 1.65, 95% CI 0.92 to 2.95, p-value = 0.092).

Discussion

Prior studies have shown that lower cognitive performance is associated with psychotic symptoms in youth, including lower visual memory performance (Cullen et al., 2010; MacKenzie et al., 2017). In the present study, we examined the relationship between visual memory performance and psychotic symptoms in a cohort enriched for offspring of parents with mood and psychotic disorders. We found that lower visual memory performance was associated with increased likelihood of experiencing psychotic symptoms. This relationship did not change when we accounted for intelligence, demonstrating that the relationship between visual memory performance and psychotic symptoms is independent of general cognitive ability.

We found that lower visual memory performance was associated with psychotic symptoms in children, adolescents and young adults. Previous research using questionnaire measured psychotic-like experiences reported a moderate relationship between lower visual memory performance and psychotic symptoms that was not statistically significant (Cullen et al., 2010). This apparent discrepancy may reflect the differences in quality of assessment of psychotic symptoms when using interview measures with curation by independent raters versus questionnaire measures that are likely to capture sub-clinical psychotic-like experiences. While questionnaires may capture a broader spectrum of psychotic-like experiences, they do not allow false positives to be identified and excluded from analyses. Our results are consistent with the lower visual memory ability that has been observed among individuals with first episode psychosis (Addington & Addington, 2002), bipolar disorder (Ha et al., 2012), schizophrenia (Grimes et al., 2017), and depression (Hammar & Schmid, 2013). Our results suggest that visual memory may represent an indicator of cognitive vulnerability to mental illness that is present among youth who

are already experiencing psychotic symptoms, which is a known indicator of risk (Fisher et al., 2013).

Our finding that visual memory performance is associated with psychotic symptoms in children, adolescents and young adults may have implications for both research and clinical care. This association between lower visual memory and definite psychotic symptoms measured through validated interview measures is a novel finding. The present study is the first to use the RCFT to measure visual memory among youth with psychotic symptoms. Future studies may consider using the RCFT to assess visual memory based on its ability to discriminate between youth with and without psychotic symptoms. The difficulty of the RCFT may contribute to its ability to discriminate between youth with and without psychotic symptoms as recalling the figure also relies on other cognitive processes (e.g. constructional ability and executive functioning) (Meyers, J. & Meyers, K., 1995). Visual memory scores from the RCFT may be a useful tool for allocation to potential clinical interventions aimed at preventing mood and psychotic disorders.

The present study benefits from a large well assessed sample of offspring of parents with and without mood and psychotic disorders. Particularly, we benefit from a thorough assessment of psychotic symptoms with all participants using interview measures. This allows assessors to prompt participants to obtain more information about potential psychotic symptoms. Only psychotic symptoms rated as “definite” through independent curation by experts were used in analyses which strengthens the certainty of our findings. Future studies may examine the longitudinal relationship between visual memory and psychotic symptoms in youth similar to previous literature examining other cognitive domains and psychotic symptoms (Niarchou et al., 2013). The RCFT was scored by one rater who was blind to the outcome, allowing for consistent and unbiased scoring of the RCFT throughout our sample. However, our results should be

interpreted in the context of several limitations. Most notably, our results are limited by a relatively low number of participants with definite psychotic symptoms. Thus, we have limited statistical power and our results require replication. Additionally, due to practice effects, the RCFT cannot be administered multiple times to the same participants. Thus, if we decided to explore repeated testing of visual memory with the RCFT (Meyers, J. & Meyers, K., 1995) it is unclear how many years we would need to wait. The Modified Taylor Complex Figure was designed to assess similar domains for repeat testing of the RCFT and may perform similarly (Hubley & Tremblay, 2002), but is less established than the RCFT. Future studies may examine reliability and sensitivity of repeated measures of visual memory using different complex figures in children and adolescents.

In conclusion, we found that among children, adolescents and young adults, lower visual memory ability was associated with increased likelihood of experiencing psychotic symptoms. Future studies may explore the relationship between visual memory and other known risk factors for major mood and psychotic disorders. Our findings may inform future targeted early interventions for youth at risk of mood and psychotic disorders.

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Disclosure of interest

The authors report no conflicts of interest.

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Table 1. Demographic and clinical characteristics of youth with and without psychotic symptoms. We tested differences between groups using X^2 (for categorical variables) and t-tests (for continuous variables).

	No psychotic symptoms (n = 183)	Psychotic symptoms (n = 22)	X^2	p-value
Females, n (%)	94 (51.37)	14 (63.64)	1.77	0.184
Offspring diagnosis, n (%)				
ADHD	33 (18.03)	9 (40.91)	6.31	0.012
ASD	9 (4.92)	3 (13.64)	2.71	0.100
Major depressive disorder	24 (13.11)	4 (18.18)	0.43	0.513
			t-statistic	p-value
Age, mean (SD)	13.14 (4.23)	12.09 (4.28)	1.09	0.138
IQ, mean (SD)	105.60 (12.66)	105.82 (13.30)	-0.08	0.530

Table 2. Effect visual memory on psychotic symptoms in youth. Logistic mixed-effects regression results. Dependent variable is 'any definite psychotic symptom'. Visual memory is inverse-z-scored so that odds ~~ration~~ ratio greater than one reflect the association of worse visual memory with psychotic symptoms.

	Odds ratio	95% confidence interval lower	upper	p-value
Visual memory	**1.80**	**1.06**	**3.06**	**0.030**
Age (years)	0.93	0.83	1.05	0.248
Sex (female)	0.62	0.24	1.59	0.321
Constant	0.26	0.06	1.13	

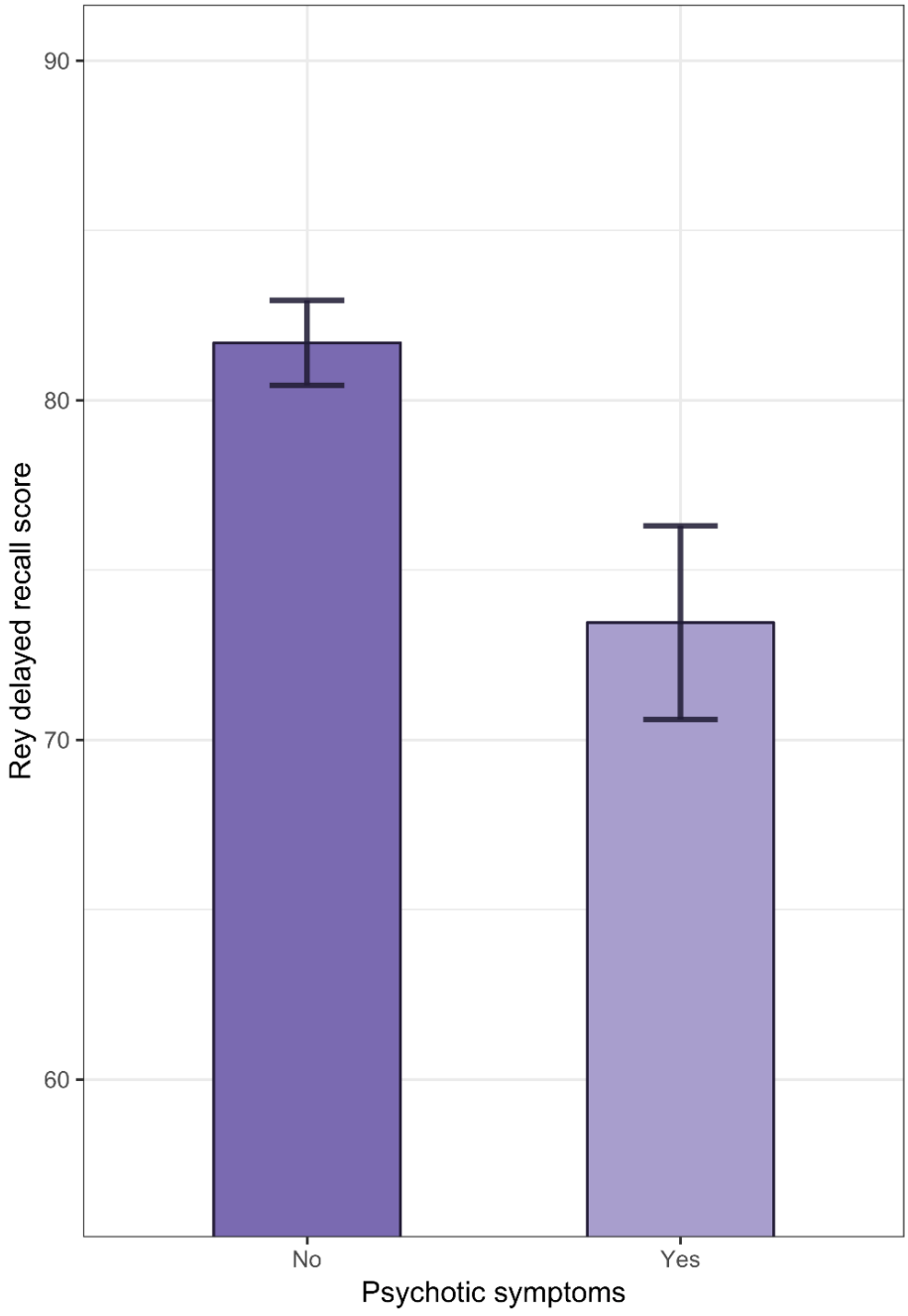

Figure 1. The mean age-standardized RCFT delayed recall scores for participants with and without psychotic symptoms. Error bars represent standard error of the mean.